The AMBRI Biosensor

CDC/DARPA Seminar Day

Executive Summary

Goal

To extend the AMBRI Biosensor to Bacterial Detection for BWD Applications

Requirements

Sensitivity:	**Bacteria 100 per ml ; toxins < 20ng/L**
Stability:	**One month at 40^{o}C**
Multi-analyte:	***E.coli*, *L.innocua*, *Y.pestis*, *B.anthracis*,**

Deliverables

- **Design rules for silicon chip biosensor**
- **Process parameters for microelectrode array fabrication**
- **Design specifications for a commercial bacteria sensor**

Project Status

Complete

- Flow cell complete and tested
- Electrode array process developed
- 96 sensor electronic chip designed, fabricated & tested
- UV flow cell constructed for photo-patterning
- Differential flow cell trials
- Caged biotin molecules synthesised for photo-patterning
- Bacteria fragmentation .optimised for improved sensitivity
- Membrane stabilising molecules synthesised
- Bacterial sensing demonstrated in a flow cell
- Sensitivity (1000 bacteria/ml) TSH (< 0.02mIU/L)

Progress to Date

Pending

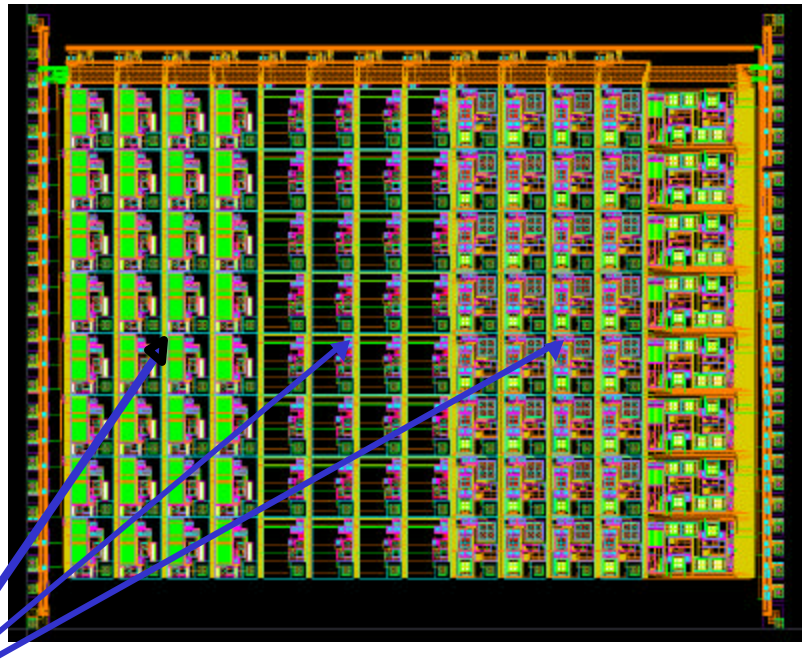
- Final testing of *E.coli*, *B.anthracis, F.tularensis, C.burnettii, Y.pestis*
- (subject to availability of high affinity antibodies)

Technology Transferred to Commercial Development

- Storage trials
- Interference trials

Electronics & Chips

0.6mm TLM CMOS
6mm x 8mm
96 sensors
32 of each amp.
8 SD converters

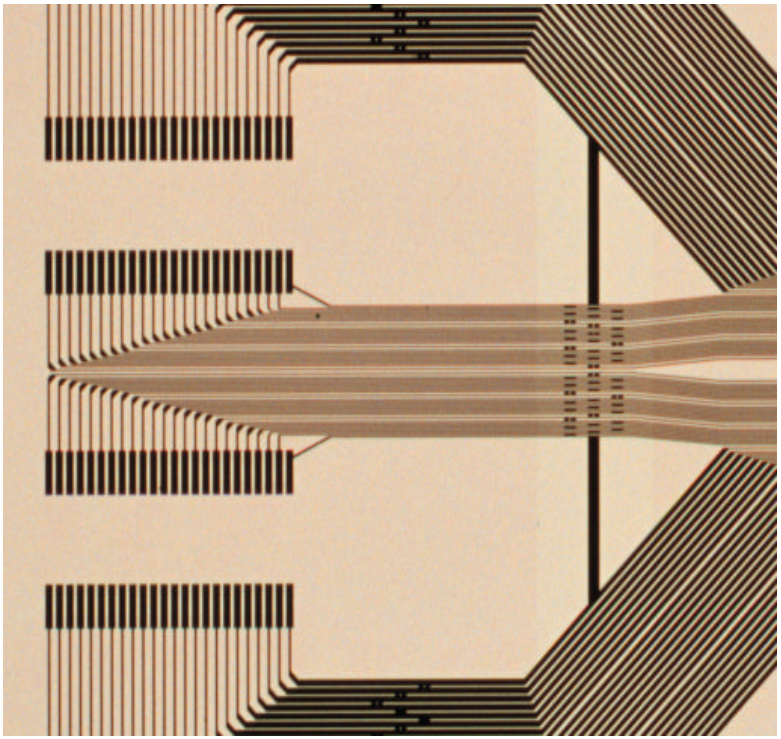


Three forms of amplifier (32 each) to test the best amplification format

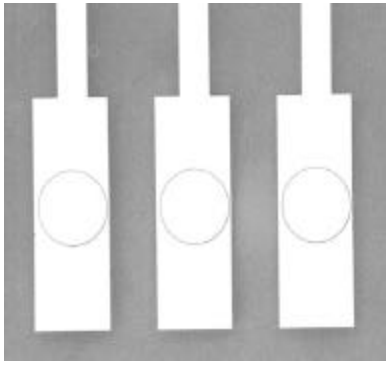
Eight x Sigma delta convertors allow parallel analog to digital conversion

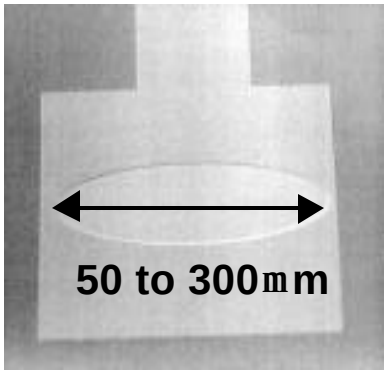
Fine Detail of Sensor Substrate

Flow cell array



Sensor pads



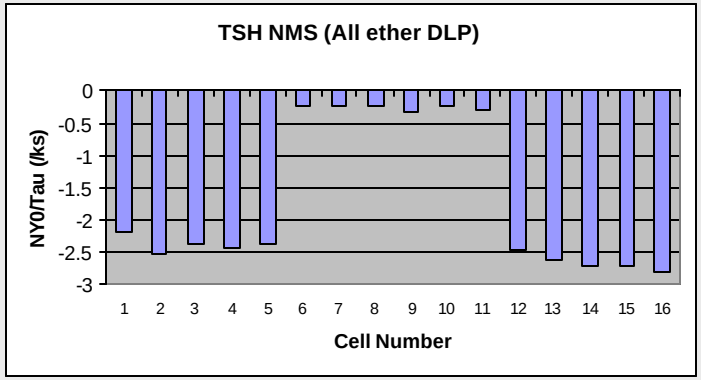


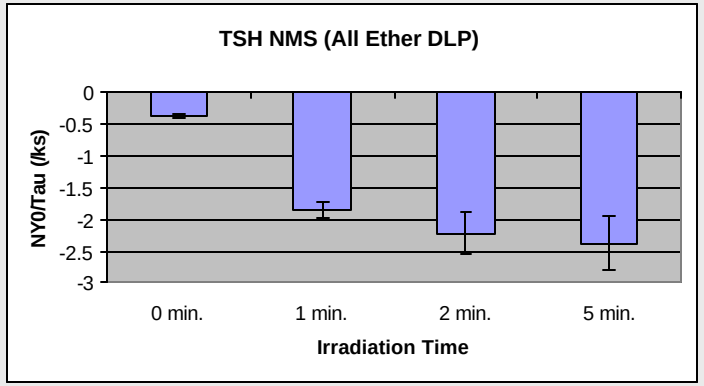
UV Caged Biotin Results

Comparison of analogues

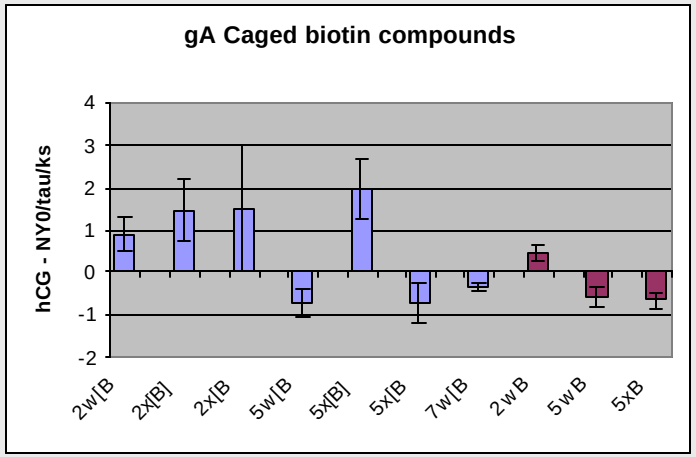
Irradiation times

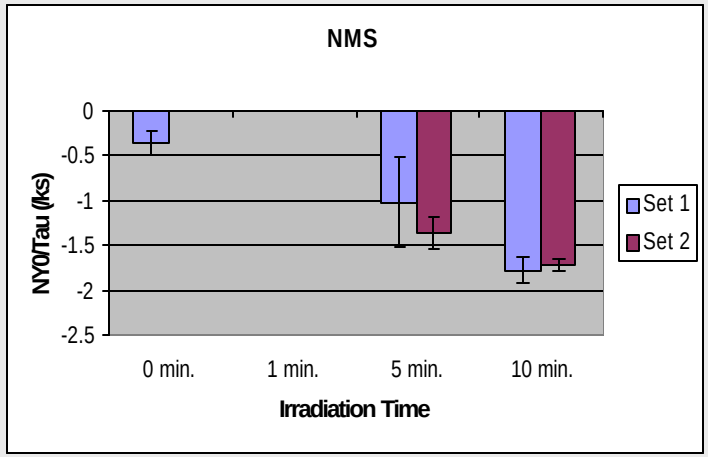
Membrane spanning lipid





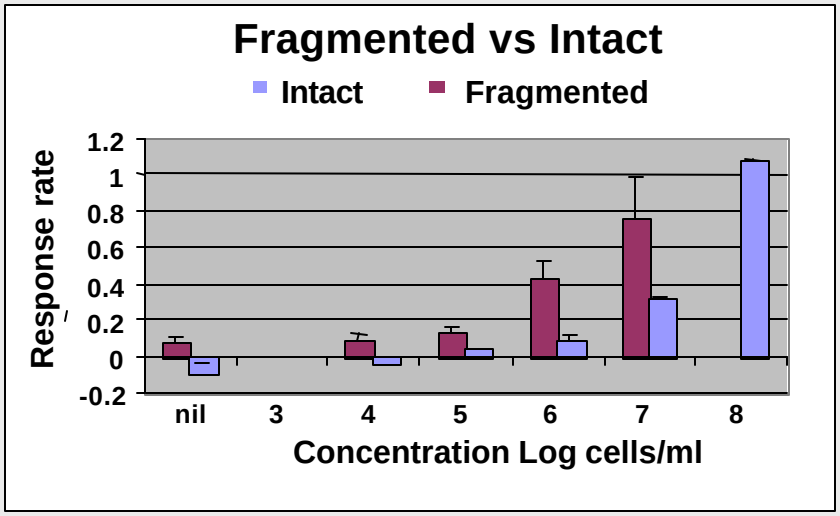
Gramicidin channel

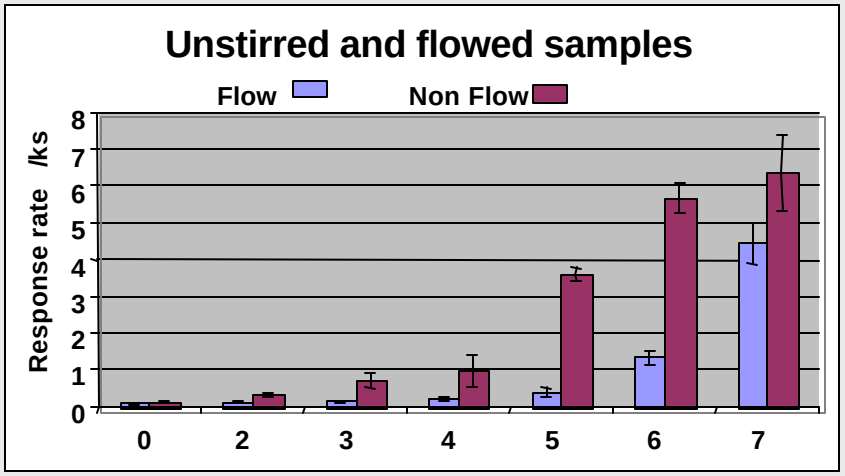


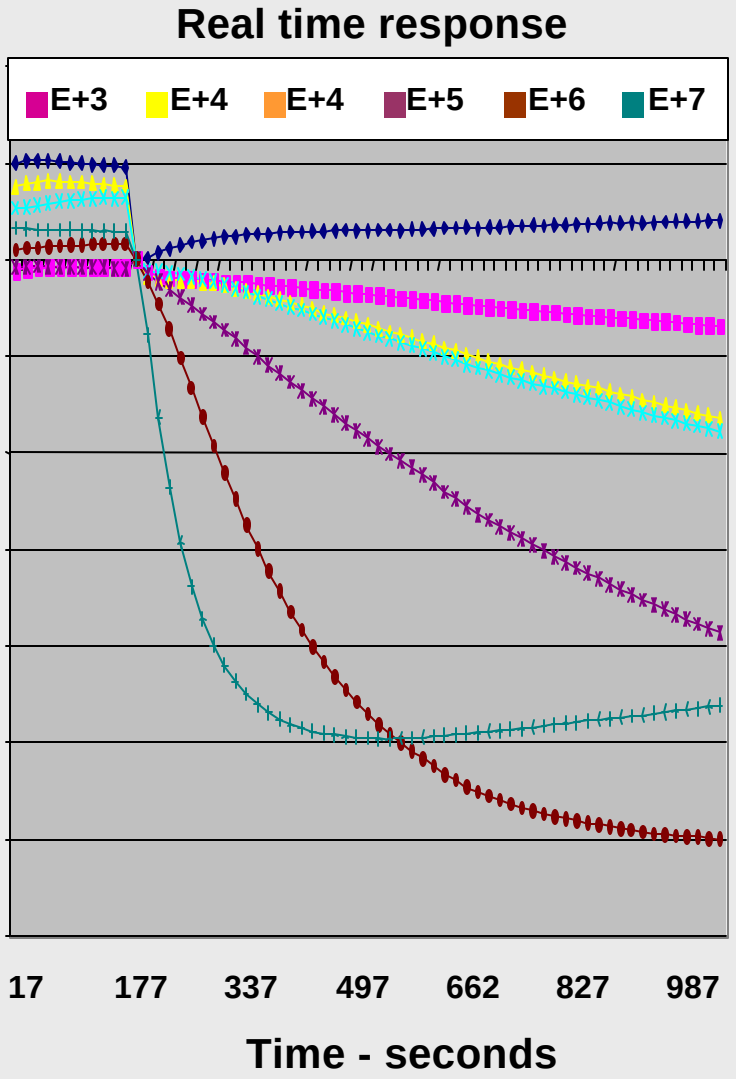


Sample Flow & Fragmentation

Ecoli titration 10^2 to 10^7 cells/ml - work in progress







Project End

goals/milestones/expectations

- **Design rules for integrated circuit biosensor chip**
- **Process control parameters for microelectrode array fabrication**
- **Draft specifications for a commercial bacterial sensor**

- **Relevant design principles integrated with medical diagnostic production**

Envisioned Deliverable
Physical & Operational Requirements

- **Robustness to Environmental Conditions**
  - Ambulances
  - Field operations (biologicals)
- **Shelf Life**
  - 1 year at ambient conditions
- **No Media Requirements**
- **Mobility (Field or Lab)**
  - Notebook sized instrument with external power
  - Defense unit could be handheld with integral power
  - Disposable is size of a business card
- **Sample processing requirements**
  - No external sample processing required

Envisioned Deliverable Detection/Performance Capabilities

- **Detection Limit** - **<** 1000 cells/ml at this time
- **Response Time** - Five minutes
- **False alarm rates** - Analyte & Format dependent

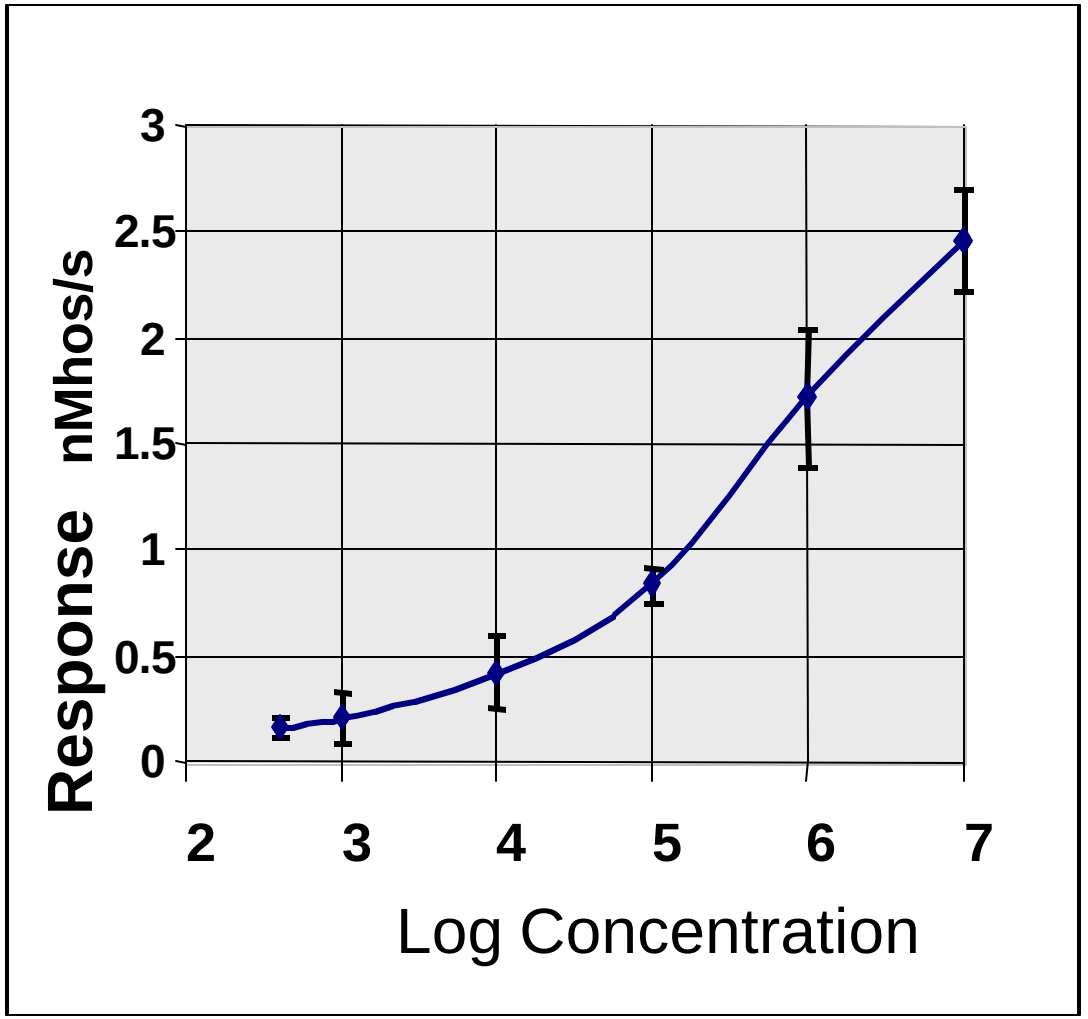
  Typical Targets

  sensitivity - 95%

  specificity - 95%

Dose Response *E.coli*

(Fragmented with flow cell)



Which Chemical Agents?

ANALYTES DETECTED TO DATE

- **Hormones & Proteins:** TSH, HCG, T4, Ferritin,
- **Nucleic acid** DNA fragments
- **Drugs & small molecules:** Digoxin, DNP
- **Organisms:** E.coli (principal model organism) Y.pestis, L.innocua, B.anthracis, Cryptosporidium, Giardia
- **Electrolytes:** potassium, sodium, chloride
- **Antibodies:** anti-TSST

Can detect/identify/classify

any agent to which a suitable ligand can be found

Summary

Applications of Envisioned Deliverable

- Any immunoassay with a sensitive response in minutes
  Continuous monitoring of an environment
  Rapid screening of a population exposed to an infectious agent

What are the unique capabilities of the AMBRI sensor

- Rapid, sensitive assay within minutes
- Small, compact, cheap and robust
- electrical format reduces matrix attenuation of signal

What are the challenges to overcome

- Rapid development of high affinity (high on rate) antibodies
- In line bacterial disruption